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Non-contrast Computed Tomography is Comparable to Contrast-enhanced Computed Tomography for Aortic Volume Analysis after Endovascular Abdominal Aortic Aneurysm Repair

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Abstract *Objectives:* To evaluate whether non-contrast computed tomography (NCCT) images are as reliable as contrast-enhanced computed tomography (CECT) images for the measurement of aortic volume (AV).
Materials and Methods: A total of 316 pairs of AVs were retrospectively measured from 316 consecutive patients, who underwent endovascular aneurysm repair (EVAR). A standardised multidetector computed tomography protocol was used to obtain precontrast, arterial and delay-phase images. A single blinded, experienced observer measured the AV from the lowest renal artery to the aortic bifurcation by means of the disc-summation method, using the pre-contrast and arterial-phase images. A second blinded observer measured the AV again in 16 randomly chosen cases.
Results: Both NCCT and CECT yielded similar AVs that were highly correlated ($r^2 = 0.99$; $P < 0.0001$). Bland and Altman analysis revealed a small bias (mean $\pm$ 2 standard deviations: -0.9 ± 8 ml). The intraclass correlation coefficients (all >0.99; $P < 0.0001$) and low repeatability coefficients indicated that the AVs were reproducible with both methods.
Conclusions: The AVs measured from NCCT images were accurate and highly reproducible compared with those from CECT images. Therefore, NCCT can be a reasonable alternative to CECT for AV assessment after EVAR. This is particularly important for patients with renal

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insufficiency (potentially sparing them from nephrotoxic contrast agents and unnecessary radiation) or allergy to contrast agents.

Introduction

Recent studies have suggested that endovascular aneurysm repair (EVAR) is a reasonable alternative to the surgical repair of abdominal aortic aneurysms (AAAs).[1,2] After EVAR, diligent follow-up testing is required to assess the residual aneurysmal size, as well as the position and integrity of the endograft. Various non-invasive imaging modalities — including plain radiography, ultrasonography, magnetic resonance imaging and computed tomography (CT) — are available for this purpose. Contrast-enhanced CT (CECT) assesses all the above variables well and is the method of choice in patients with satisfactory renal function.[3]

In the long-term follow-up assessment of these patients, the most frequent complication is endoleak, particularly type II endoleak (retrograde flow into the aneurysm sac via patent collateral vessels).[4] Type I endoleak (an incomplete seal at the proximal or distal attachment site of the endograft) and type III endoleak (an endograft fracture, modular separation or tear) almost always require repeat interventional procedures. However, many type II endoleaks are found to have resolved spontaneously on further follow-up examinations;[5] hence, other factors should be taken into consideration before a decision for re-intervention is made. With certain types of endografts, increased permeability of the graft material occasionally results in an increased AAA size (i.e., endotension or type V endoleak) without evidence of endoleak. In this patient population, the increased AAA size and endotension could lead to rupture. Long-term analysis of the aortic volume (AV) with CECT is helpful in assessing the severity of endoleak and in indicating the need for early treatment.[5–11] Patients with AAAs tend to be elderly, and frequently have associated renal insufficiency (a relative contraindication for intravenous iodinated contrast administration). Because non-contrast computed tomography (NCCT) does not necessitate the use of potentially nephrotoxic, iodinated contrast agents and unnecessary radiation during EVAR follow-up evaluation, we investigated whether NCCT is comparable to CECT for assessing the AV.

Materials and Methods

Patients

Retrospective analysis of the cardiovascular CT registry at our hospital revealed 316 consecutive patients, who had EVAR from 1 January 2005 to 1 January 2006, and who underwent follow-up CECT assessment. This study was approved by our institutional review board.

Imaging techniques

The images were acquired with either a 16- or a 64-detector CT scanner (Siemens Medical Systems, Forchheim, Germany; Philips Medical System, Best, the Netherlands; and General Electric Medical Systems, Milwaukee, Wisconsin, USA). A standardised protocol was followed, and non-contrast, arterial and delayed images were obtained for all patients. The delayed images were acquired 30 s after the arterial images, which were not used for this analysis; only the NCCT and CECT images were analysed. A representative scanning protocol for a typical patient included the following steps:

(1) Non-contrast images were obtained from the level of the diaphragm to the level of the femoral heads. With the 16-slice scanner, we used a slice thickness of 3 mm; collimation of 1.5 mm; rotation time of 0.5 s; pitch of 0.45; beam energy of 120 kVp; and an effective tube current of 250 mAs. With the 64-slice scanner, we used a slice thickness of 3 mm; collimation of 1.2 mm; rotation time of 0.5 s; pitch of 1.4; beam energy of 120 kVp; and an effective tube current of 160 mAs.
(2) The delay time was obtained by means of the test bolus technique after 20 ml of ioversol (Optiray) contrast agent (Covidien, Mansfield, MA, USA) was injected at a concentration of 320 mg iodine ml^{-1}, followed by a 40-ml bolus of normal saline with a flow rate of 4 ml s^{-1}. The delay time was obtained by using the built-in analysis software supplied by each CT vendor.
(3) Arterial images were obtained by using 100 ml of contrast material followed by 80 ml of normal saline at 4 ml s^{-1}, starting at the level of the diaphragm and extending to the level of the femoral heads. With the 16-slice scanner, we used a slice thickness of 3 mm; collimation of 1.5 mm; rotation time of 0.5 s; pitch of 0.5; beam energy of 120 kVp; and an effective tube current of 200 mAs. With the 64-slice scanner, we used a slice thickness of 3 mm; collimation of 1.2 mm; rotation time of 0.5 s; pitch of 0.75; beam energy of 120 kVp; and an effective tube current of 275 mAs.
(4) Delayed images were obtained by using the same parameters used to acquire the arterial images, but the delayed images covered only the endograft to detect any endoleak. All images were reconstructed by using a medium-smooth kernel.

Measurement of AV

The CT data were transferred to a commercially available workstation (Vitrea™; Vital Images, Inc., Minnetonka, Minnesota, USA) for analysis. An experienced observer (with 6 months of dedicated vascular CT training) then assessed each image to determine the AV. The measurements were made in random order without the observer knowing the patients' names or clinical data. With both NCCT and CECT images, the AVs were measured by means of the disc-summation method. Aortic contours were drawn on the

most external aspect of the aortic wall and included any aortic thrombus; the contours were drawn empirically, beginning immediately below the take-off of the lowest renal artery and terminating at the aortic bifurcation, where the common iliac arteries begin (Fig. 1). After at least 4 weeks, intra-observer variability was assessed in 16 randomly chosen cases. Similarly, inter-observer variability was evaluated by another experienced observer (with 3 years of experience in vascular CT) in another 16 randomly chosen cases. Assessment of changes in the aortic diameter in the serial CT examinations was not part of this current investigation.

Statistical analysis

Variables were expressed as the median value with lower and upper quartiles. The Wilcoxon rank-sum test was used to compare the AVs obtained with NCCT versus CECT. The results were assessed with Pearson's correlation coefficients. A *P*-value (two-sided) of <0.05 was considered significant.

To assess the agreement between the AVs obtained from NCCT versus CECT images (the latter being considered the gold standard), we used the analytic method proposed by Bland and Altman.[12] Furthermore, the coefficient of variation (CV), the ratio of the standard deviation to the mean, was computed according to the formula of McLaughlin et al..[13] The CV measures the ability to repeatedly obtain the same value for a single sample (i.e., duplicate or replicate analyses) and should be between 1% and 5%. A large CV implies that the data have great variability, whereas a small CV implies that they have only a small amount of variability.

To assess inter-observer and intra-observer reproducibility, we calculated the intraclass correlation coefficient (ICC).[14] A measure of concordance when a variable is continuous, the ICC corrects correlations for a systematic bias. The value of the ICC is between 0 and 1, where 1 signifies perfect reproducibility and 0 signifies a degree of reproducibility no better or worse than that afforded by chance. An ICC of >0.75 is considered to indicate clinical usefulness. Scatterplots using the Bland–Altman approach were also constructed. In addition, the inter-observer and intra-observer variability was assessed by using the repeatability coefficient as outlined by Bland and Altman.[12] The repeatability coefficient is computed by multiplying the standard deviation of the difference between the two measurements by 2. The coefficient should be less than 2 standard deviations of the mean measurement (obtained from the scattered plot of the Bland–Altman analysis).

Calculations were performed with a commercially available statistical analysis package (Statistical Package for Social Sciences (SPSS) 12.0; SPSS Inc., Chicago, IL, USA).

Results

A total of 316 patients were identified (282 men and 34 women; median age, 76 (69, 81) years), resulting in 316 pairs of AV measurements. A total of 244 patients (77%) had coronary artery disease, 268 patients (85%) had hypertension and 58 patients (18%) had diabetes mellitus. More importantly, 114 patients (36%) had stage 3 or worse chronic renal disease (characterised by an estimated glomerular filtration rate of <60 ml^{-1} min^{-1}/1.73 m^2).

Fig. 2 shows the types of endografts and their frequency of use. The AneuRx® (Medtronic Inc., Santa Rosa, CA, USA) and the Excluder® (W. L. Gore & Associates, Flagstaff, AZ, USA) endografts were the most frequently used systems.

There was no difference between the AVs obtained with NCCT versus CECT (median, 116 (89, 159) ml vs. 114 (89, 157) ml, respectively; $P = 0.82$). The AVs obtained with both methods were highly correlated ($r = 0.99$; $P < 0.0001$) (Fig. 3). The CV between AVs obtained from NCCT versus CECT images was 2.8%.

Fig. 4 shows the agreement between the AVs obtained from NCCT versus CECT images when analysed according to the Bland and Altman method. The AVs obtained from NCCT images underestimated those obtained from CECT images by -0.9 ml (the mean bias), with limits of agreement (mean bias $\pm$ 2 sd) between 7.1 and -8.9 ml.

Inter- and intra-observer reproducibility from a random sample of 16 patients was assessed on the basis of the ICC. The ICCs were all >0.9 (Table 1), and the repeatability coefficients were within or very close to 2 standard deviations of the mean difference (Table 2; the standard deviations are available in Fig. 5), implying that AVs obtained

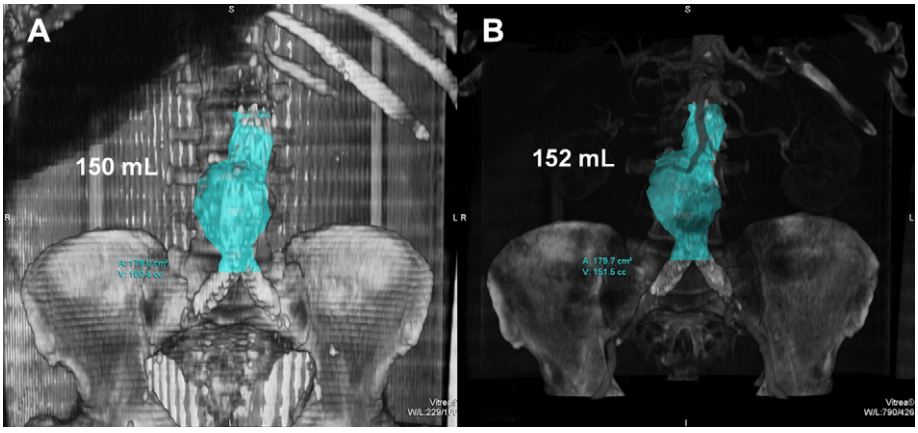

Figure 1 Aortic volumes obtained with noncontrast computed tomography (A) and contrast-enhanced computed tomography (B).

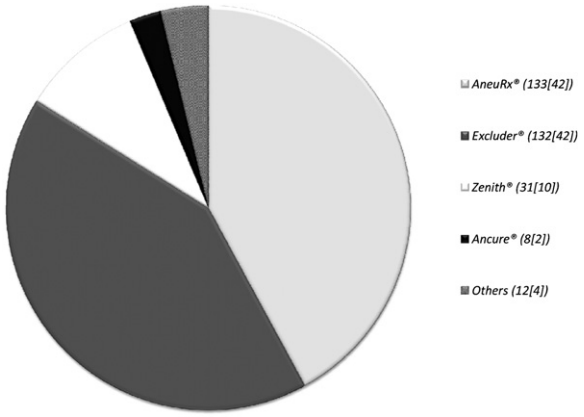

Figure 2 Types of endografts and their frequency of use (number [%]) in our patients.

with NCCT and CECT are reproducible. Fig. 5 shows the inter-observer and intra-observer variability, as analysed by the Bland and Altman method, for AVs measured with both NCCT and CECT. The AVs obtained with both methods were reproducible, the reproducibility being better in the intra-observer than the inter-observer assessment.

Discussion

Currently, there is no precise definition of what constitutes successful EVAR, but a reduced aneurysm size and an absence of endoleak are usually considered successful end points. After EVAR, close follow-up observation is necessary to detect endograft migration, endoleak and other potential complications.

Although aneurysmal diameter is a parameter that is commonly measured,[6,15,16] various authors have indicated that AV measurement is a more reliable method for following up EVAR patients.[3,6,8,17–19] Moreover, Wever et al.[20] have shown that, compared to AV measurement, assessment of the maximal diameter (using a dedicated post-processing workstation) failed to detect an aneurysmal size change in more than 33% of cases. Several

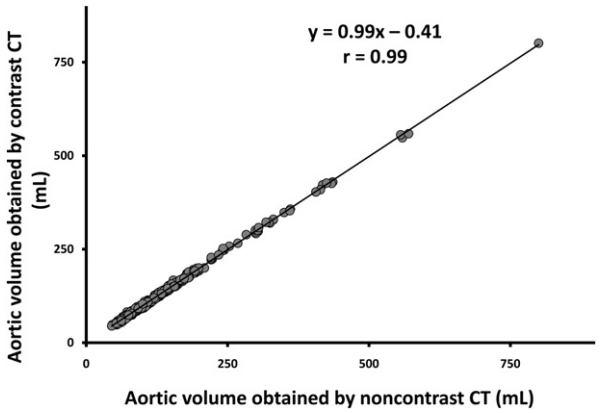

Figure 3 Correlation between aortic volumes obtained with noncontrast versus contrast-enhanced computed tomography (CT).

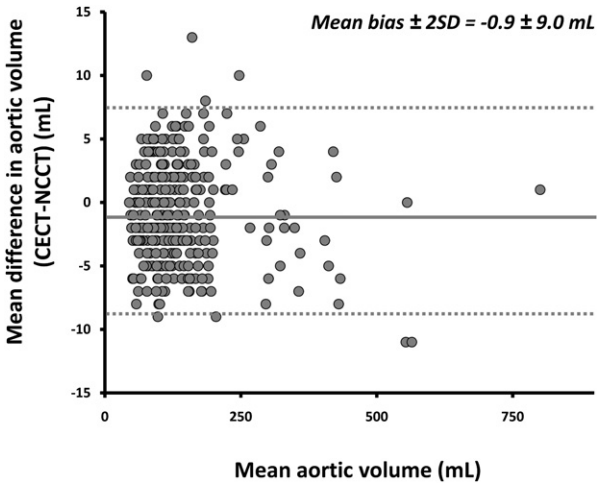

Figure 4 Bland and Altman analysis of agreement between aortic volumes obtained with noncontrast computed tomography versus contrast-enhanced computed tomography (316 pairs of data). The solid gray line represents the mean bias for the aortic volumes, and the gray dotted lines represent 2 standard deviations above and below the mean.

factors limit the usefulness of the maximal diameter in assessing aneurysmal size. Whereas the maximal diameter represents only a small segment of the aorta, AV measurement takes into account the aortic size in all three dimensions. Moreover, AV measurement is more sensitive to changes in the aortic size than is diameter measurement, especially if the change in the aortic dimension is in the longitudinal (foot-to-head) direction. In addition, the diameter is difficult to measure at exactly the same level during sequential follow-up examinations, especially when performed by different operators.

The major finding of this study is that the AV obtained with NCCT is accurate and comparable to that obtained with CECT, as reflected by the low CV (2.8%) and the small mean difference on Bland and Altman analysis (−0.9 ml), indicating extremely close agreement between the two techniques. The majority of the published studies concerning AV evaluation by means of CT have involved administration of a contrast agent.[6,8,17–20] In a recent study, Bley et al.[21] suggested that using NCCT to obtain the AV is an adequate screening test for following up EVAR patients. In addition, on the basis of our Bland and Altman analysis, we have demonstrated the reproducibility of AVs obtained with both methods: the ICC was high (>0.9), and the repeatability coefficients showed good inter- and intra-observer reproducibility. These results indicate that reliable and reproducible AVs can be obtained from NCCT images, without the administration of a contrast agent.

Our results are quite comparable to those obtained by Wever et al.[20] with regard to the repeatability coefficients for inter-observer and intra-observer variability. The lower repeatability coefficients for intra-observer versus inter-observer variability in both the NCCT and CECT studies suggest that measurements are more reliable if made by the same observer. In fact, when a previous study evaluated by a different interpreter is used for comparison during EVAR follow-up assessment at our institution, it is

Table 1 Intraclass correlation coefficient for intra-observer and inter-observer reproducibility of aortic volume measurements obtained with noncontrast and contrast-enhanced computed tomography.

Type of reproducibility	ICC (95% CI)	
	Noncontrast CT	Contrast-enhanced CT
Intra-observer	0.998* (0.994, 0.999)	0.996* (0.988, 0.998)
Inter-observer	0.998* (0.991, 0.999)	0.998* (0.994, 0.999)

ICC, intraclass correlation coefficient; CI, confidence interval; CT, computed tomography.
*$P < 0.0001$ for all ICCs.

mandatory the interpreter of the most recent study remeasure the AV from the last examination, thereby minimising discrepancy and variability.

Our study is different from the one recently reported by Bley et al.,[21] as our primary intention was to demonstrate that AVs obtained with NCCT are comparable to those traditionally obtained with CECT; clinical follow-up observation was not part of our criteria. However, Bley et al. did demonstrate the clinical usefulness of AVs obtained from NCCT in the follow-up evaluation of EVAR patients.

To the best of our knowledge, the literature contains no previous reports regarding the comparison of AVs obtained with NCCT versus CECT. There is no consensus regarding what constitutes a significant change in AV during serial measurement. Pollock et al.[8] considered a 10% change in the AV, compared to the previous AV, as significant. In the study by Wever et al.,[20] the lowest repeatability coefficient for the AV was 3.2%, meaning that if the AV change exceeds the repeatability coefficient, the volume change can be considered significant, with a confidence interval of 95%; our data correspond well with theirs. Furthermore, Bley et al.[21] used 2% as their cut-off, based on their early work.

Due to the retrospective nature of the analysis, as well as the non-objective nature of this study, the effective radiation dose that each patient received was not documented. However, for a typical male patient weighing 80 kg, the total dose-length product for a follow-up scan with precontrast, arterial and delayed-phase images was approximately 636, 736 and 389 mGy cm, respectively, with a 16-slice CT scanner. When we used a conversion factor of 0.017 mSv mGy^{-1} cm^{-1}, the effective dose was 10.8, 12.5 and 6.6 mSv, respectively. For a typical female patient weighing 80 kg, the effective dose was approximately 11.9, 12.3 and 5.1 mSv, respectively, for precontrast, arterial and delayed-phase images. These results compared favourably to those obtained by Macari et al.,[22] taking into account that Macari's results were the average effective dose and that the acquisition technique differed slightly between the two studies.

Obtaining the AV by prescribing the contours manually could be a time-consuming process. Although we did not formally assess the time it took to obtain an AV in this study, we estimated that the AV can be comfortably obtained within 3–5 min by an experienced operator.

In the long-term follow-up assessment of EVAR patients, NCCT may have an important role in obtaining the AV.[6] In a recent systematic review, 23–36% of patients aged 64 years or older were estimated to have chronic kidney disease (CKD), defined as a glomerular filtration rate of <60 ml $min^{-1}/1.73$ m^2.[23] Furthermore, CKD is a well-known risk factor for contrast-induced nephropathy.[24] In individuals who have CKD, NCCT could be a reasonable alternative to CECT for obtaining the AV, therefore avoiding the use of potentially nephrotoxic contrast agents and further deterioration of renal function. This approach could also apply to patients with preserved renal function; for those who have a stable or continual reduction in AV, as measured by NCCT, the administration of a contrast agent would not be necessary. In fact, this is exactly what Bley et al. concluded.[21] Moreover, NCCT avoids the additional radiation that is necessary during arterial and delayed-phase imaging.[21] Without the use of an iodinated contrast agent, it could be difficult to detect a type I endoleak with NCCT. Furthermore, a subtle type III endoleak could also be difficult to detect with CT due to the underlying beam-hardening artefact, although the use of a contrast agent should help identify the location of the defect. When NCCT is used to follow-up EVAR patients, plain radiography could be a useful non-invasive modality for detecting stent migration or fracture.[25]

At our institution, EVAR patients undergo CECT imaging at 1, 6 and 12 months and yearly thereafter for surveillance of the endograft, if no endoleak is identified. Since late 2005, measurement of the AV has been a standard component of the CT angiography report provided to the ordering physician. Patients with stages IV and V CKD and selected patients with stage III CKD (especially those who have diabetes mellitus) are imaged only with NCCT. The result is carefully compared with the AV from previous studies to detect a significant interval change. Other auxiliary techniques used in patients with renal insufficiency include plain radiography and duplex ultrasonography.[26]

Table 2 Repeatability coefficients for aortic volumes.

	Inter-observer		Intra-observer	
	NCCT	CECT	NCCT	CECT
Aortic volume (ml)	10.7	9.0	3.7	5.5

NCCT, noncontrast computed tomography; CECT, contrast-enhanced computed tomography.

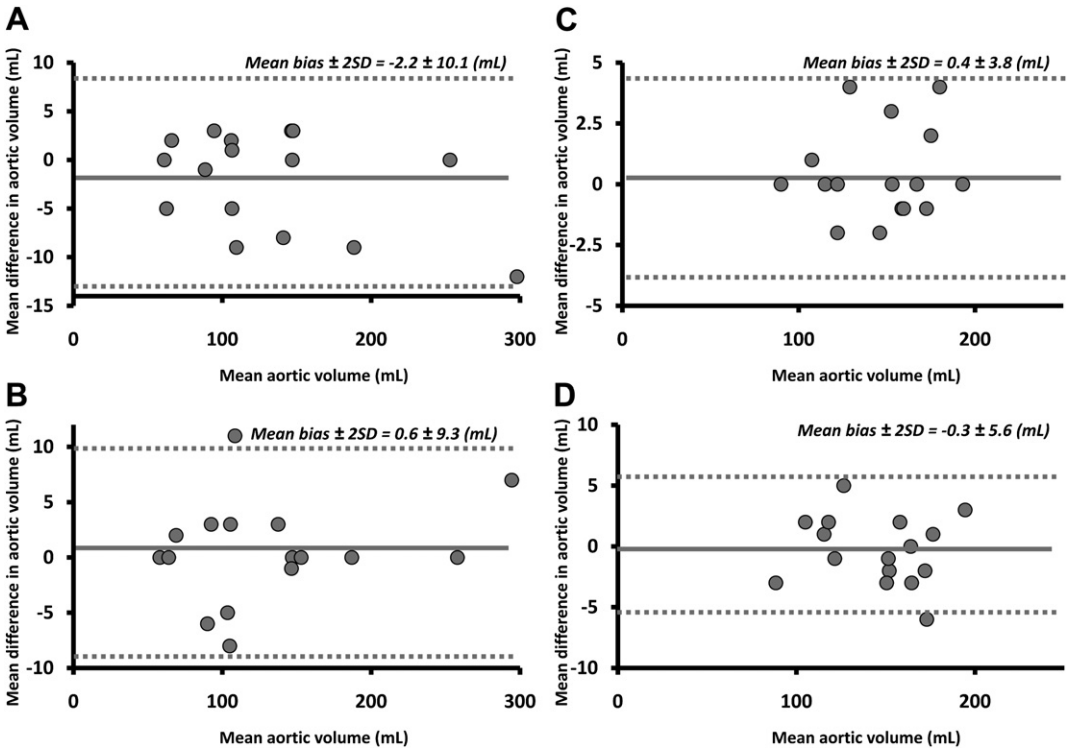

Figure 5 Bland and Altman analysis of inter-observer variability in the measurement of aortic volumes (AVs) obtained with noncontrast computed tomography (NCCT) (A) and contrast-enhanced computed tomography (CECT) (B) and of intra-observer variability in the measurement of AVs obtained with NCCT (C) and CECT (D). In A, there are 2 values [(147.5, 3) and (146.5, 3)] that are in extremely close proximity to one another in the horizontal axis (mean aortic volume). Similarly, in C, there are 2 values in very close proximity to each other [(158.5, −1) and (159, −1)].

Limitations

In NCCT images, the proximal margin (at the level immediately below the lowest renal artery) could potentially be difficult to locate; with careful inspection, however, this area can be identified in most cases. In the current study, we demonstrated that AVs measured from NCCT images are comparable to those measured from CECT images. Nevertheless, the use of NCCT alone to provide the AV, in conjunction with other non-invasive modalities (e.g., plain radiography), in the follow-up of EVAR patients was not tested, and its value remains to be proven. The AVs obtained in this study were assessed by experienced operators at an institution with a very high volume; in the near future, the availability of fully automated algorithms in dedicated post-processing workstations may limit user variability, enhance accuracy and reduce the time needed for AV measurement.

Conclusions

Our data indicate that in the follow-up evaluation of EVAR patients, the AV obtained from NCCT images is accurate and highly reproducible when assessed by experienced observers, with low inter- and intra-observer variabilities compared with the AV obtained from CECT images (the gold standard). By using NCCT, physicians could potentially avoid the use of iodinated contrast agents in a number of EVAR patients, many of whom have CKD; contrast agents would be administered only to patients who had a significantly changed AV during follow-up testing. This approach would also spare patients the additional radiation necessary during the arterial and delayed phases of CT angiography.

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Conflict of interest/Funding

None.

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